

Appl. No.: 10/690,462
Amendment dated April 3, 2006
Reply to Office Action of November 3, 2005

REMARKS

Reexamination and reconsideration of this Application, withdrawal of the rejections, and formal notification of the allowability of all claims as now presented are earnestly solicited in light of the above claim amendments and remarks that follow.

Claims 13, 23, and 26 have been amended to more clearly recite that the carboxylic acid, carboxylic ester, and carboxamide substituents recited therein are groups, and have further been amended to remove H and alkyl (claim 26 only) from the group from which R₁ is selected. Claim 26 has further been amended to specifically recite the types of cancer from which the recited cancerous tissue is selected. Claims 36-38 have been amended to harmonize the language thereof with the remaining claims. Support for these amendments can be found throughout the specification as filed and particularly at pages 3-8, 12 and 47-52. Applicants respectfully submit no new matter has been added by the present amendments. Claims 18-19, 21-22, 24-25, 31-32, and 34-35 have been canceled without prejudice or disclaimer, and Applicants reserve the right to file continuing applications to claim the cancelled subject matter.

New claims 39-63 have been added, said new claims finding support throughout the specification and the previously filed claims. New independent claim 39 finds support in the combination of previous claims 13 and 18. New independent claim 46 finds support in the subject matter of previously filed claim 23. New independent claim 49 finds support in the subject matter of previously filed claim 26 and pages 12 and 47-52 of the specification. New independent claims 60 and 62 likewise find support at pages 12 and 47-52 of the specification, in addition to previously filed claims 36 and 37, respectively. Claims 13-16, 20, 23, 26-30, 33, and 36-63 are pending in the present application.

Rejections Under 35 U.S.C. §112

Claims 13-38 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In particular, the Office argues recitation of "carboxylic acid, carboxylic ester, and carboxamide" in definition of X₁ and X₂ renders the claims indefinite as it is not clear whether they are recited as compounds or groups. Applicants respectfully traverse this rejection.

The Office Action alleges "carboxylic acid, carboxylic ester, and carboxamide" are used in definition of X₁ and X₂; however, Applicants respectfully note this is incorrect. Actually,

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"carboxylic acid, carboxylic ester, and carboxamide" are part of the group of substituents recited as being optionally substituted on each carbon atom of the heteroaryl rings. In other words, "carboxylic acid, carboxylic ester, and carboxamide" are incorporated in the recited grouping of substituent groups that can optionally be substituted on a ring carbon atom. One of skill in the art would clearly recognize the use of the phrase "substituted with a substituent selected from the group consisting of" (as used throughout the claims) to indicate that the elements recited thereafter are intended as substituting groups, not independent compounds.

In light of the clear language in the claims reciting a group of substituents, Applicants do not understand how the Office can reasonably view the language as indefinite. Rather, Applicants believe the previous claim language would be viewed as clear and definite by one of skill in the art. Nevertheless, in order to expedite prosecution, Applicants have amended the claims to more clearly recite "a carboxylic acid group, a carboxylic ester group, and a carboxamide group." Accordingly, Applicants submit the claims are clear and definite, and Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 26-38 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure in relation to the treatment of cancer generally. Applicants respectfully traverse this rejection.

Initially, Applicants redirect the attention of the Office to the statements provided in Applicants' response of August 24, 2005, wherein Applicants specifically noted portions of the present application supporting treatment of cancer generally, as well as previous citations in the art supporting treatment of cancer of generally. To this end, Applicants further direct the attention of the Office to page 2917 (right column) of El-Subbagh *et al.* (*J. Med. Chem.* 2000, 43, 2915-2921), which the Office solely relies upon in the further rejections discussed below. Therein, El-Subbagh *et al.* teach that compounds can have "broad-spectrum antitumor" activity. In fact, El-Subbagh *et al.* teach that several of their compounds have broad-spectrum antitumor activity based upon activity against only a small number of specific cancer cell lines.

In light of the above, Applicants respectfully submit that the present specification is enabling for the treatment of cancer, as previously claimed. Nevertheless, to expedite prosecution, Applicants have amended independent claim 26 to recite a method of treating cancerous tissue wherein the cancerous tissue is selected from the group consisting of breast

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cancer, colon cancer, prostate cancer, skin cancer, leukemia, non-small cell lung cancer, CNS cancer, ovarian cancer, and renal cancer. To this end, Applicants direct the attention of the Office to pages 47-52 of the specification wherein activity against the recited types of cancer is supported by experimental data. Applicants also direct the attention of the Office to page 12 of the specification where treatment of specific cancer types is further disclosed.

In light of the above, Applicants respectfully submit the present rejection of claims 26-38 is inapplicable. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Applicants further respectfully submit that new claims 60 and 62, are fully enable, said claims reciting methods of treating cancerous tissue comprising administering to a subject an effective amount of a compound, as defined in the claims. In particular, claim 60 recites a method wherein the effective amount comprises an amount sufficient to inhibit VEGF production in the cancerous tissue. Similarly, claim 62 recites a method wherein the effective amount comprises an amount sufficient to inhibit TF production in the cancerous tissue.

Applicants specifically direct the attention of the Office to page 13 (lines 1-14) of the specification, which describes the believed function of the inventive method for treating cancer by inhibiting angiogenesis in cancerous tissue, resulting, in part, from inhibition of TF and VEGF production in the tissue. Accordingly, Applicants respectfully submit new claims 60 and 62 are fully enabled by the specification.

Rejections Under 35 U.S.C. §102

Claims 26-28, 31, 34, 35, and 38 stand rejected under 35 U.S.C. §102(b) as being anticipated by El-Subbagh *et al.*, *J. Med. Chem.* (2000) 43:2915-2921. Applicants respectfully traverse the present rejection.

Initially, Applicants respectfully submit El-Subbagh *et al.* is inappropriately cited as a reference under 35 U.S.C. §102(b). Such was previously raised by the Applicants in the response dated August 25, 2005. The Office now argues "the subject matter embraced in the paper has been in the public domain as it was presented in a meeting held at Saudi Arabia." Applicants respectfully submit the Office is confusing the standards under 35 U.S.C. §102.

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To be a reference under 35 U.S.C. §102(b), the publication date of the document must be at least one year prior to the filing date of the present application. The present application enjoys an effective filing date that is at least as early as December 4, 2000 (the filing date of Application No. 09/729,662, of which the present application is a continuation). The only publication date provided in the El-Subbagh *et al.* paper is the web publication date of July 7, 2000. This date is not at least one year prior to the effective filing date of the present application.

To support its rejection, the Office points to the 1999 presentation in Riyadh, Saudi Arabia, as noted in the footnote of the paper. This footnote in no way provides a concrete publication date and certainly does not support publication of the complete disclosure of the present El-Subbagh *et al.* paper prior to the web publication date of July 7, 2000. Accordingly, El-Subbagh *et al.* is improperly cited as a reference under 35 U.S.C. §102(b), and Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants do note the Office's allegation that the mention in the footnote of the 1999 Riyadh disclosure puts the publication in the public domain. Such a public domain allegation is not a basis for a §102(b) rejection. Accordingly, Applicants view such an argument as relating to §102(a). Applicants still submit, though, that the 1999 Riyadh disclosure is inconsequential. First, the footnote specifically states the subject matter of the paper was "presented in part." El-Subbagh *et al.* only disclose a single compound (compound 13) upon which the Office relies in making its rejections. The Office has provided absolutely no evidence that the "part" of the paper that was presented in the 1999 Riyadh disclosure even included compound 13.

Second, for a public disclosure to be considered novelty-destroying under §102(a), the disclosure must be made "in this country." The court in *In re Ekenstam*, 256 F.2d 321, 118 (CCPA 1958) held that prior knowledge or use which is not present in the United States, even if widespread in a foreign country, cannot be the basis of a rejection under 35 U.S.C. §102(a). The Office argues the 1999 Riyadh presentation put the paper in the public domain; however, the Office has provided no evidence of a disclosure in the United States prior to the July 7, 2000, web publication.

Third, the Office has failed to show that any portion of the partial presentation made in Riyadh was incorporated into a document that could be considered a publication under 35 U.S.C. §102(a). In other words, there is no evidence of dissemination of printed copies of the

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presentation, a poster session, or the like. Accordingly, even if the Office raises El-Subbagh *et al.* as a reference in a 35 U.S.C. §102(a) rejection, Applicants respectfully submit the Office can make no reliance on the 1999 Riyadh disclosure noted in the footnote.

Turning to the present rejections, Applicants respectfully submit that the cited claims are not encompassed by El-Subbagh *et al.* Claims 31 and 34-35 have been canceled, thereby obviating the rejection thereof. The Office has only pointed to a single compound disclosed by El-Subbagh *et al.* in making the present rejection, that being compound 13. To this end, Applicants respectfully point out that the cited claims do not encompass methods of treatment using bis(4-pyridyl) piperidone compounds where the ring nitrogen in the piperidone is substituted with a methyl group. Moreover, El-Subbagh *et al.* do not teach or suggest treating the specifically recited types of cancerous tissue using the recited compounds. Accordingly, Applicants respectfully submit the present claims are novel over El-Subbagh *et al.*, and Applicants request reconsideration and withdrawal of the present rejection.

Rejections Under 35 U.S.C. §103

Claims 13-15, 19-20, 22-23, 25-28, 30, 32-33, and 38 stand rejected under 35 U.S.C. §103(a) as being unpatentable over El-Subbagh *et al.* Claims 19, 22, 25, and 32 have been canceled, thereby obviating the rejection thereof. The Office argues the compounds encompassed by the claims only differ from the compound disclosed by El-Subbagh *et al.* by having hydrogen instead of methyl as a substituent on the piperidone ring nitrogen. Further, the Office argues such a difference is not patentably distinct. Applicants note that hydrogen has been removed in the cited claims as a possible substituent for the piperidone ring nitrogen. Applicants also respectfully submit the remaining possible substituents for the piperidone ring nitrogen are patentably distinct from the methyl substituent disclosed in El-Subbagh *et al.* Particularly, one of skill in the art would recognize that the remaining possible substituents for the ring nitrogen, as presently recited, are sufficiently structurally dissimilar from a methyl substituent such that a skilled artisan would not be motivated to make compounds including the remaining substituents and expect the compounds to possess the same utility as with a methyl substituent. Furthermore, Applicants respectfully submit the Office has failed to provide any evidence to the contrary. Accordingly, Applicants respectfully submit the cited claims are not

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obvious in light of El-Subbagh *et al.*, and Applicants request reconsideration and withdrawal of the present rejections.

Rejections Non-Applicable to New Claims

Regarding new claims 39-63, Applicants respectfully submit these claims are both novel and non-obvious over El-Subbagh *et al.* Particularly, Applicants point out that new claims 39-63 teach bis(2-pyridyl) compounds while El-Subbagh *et al.* only disclose bis(4-pyridyl) compounds. Such compounds are clearly not disclosed by El-Subbagh *et al.*, and the Office has provided no evidence to suggest a skilled artisan would find motivation or suggestion in El-Subbagh *et al.* to make such compounds. Accordingly, Applicants respectfully submit the teaching of El-Subbagh *et al.* does not anticipate or make obvious the noted new claims.

Consideration of Previously Submitted Information Disclosure Statement

It is noted that an initialed copy of the PTO Form 1449 that was submitted with Applicants' Information Disclosure Statement filed January 31, 2005, has not been returned to Applicants' representative with the Office Action. Accordingly, it is requested that an initialed copy of the Form 1449 be forwarded to the undersigned with the next communication from the PTO. In order to facilitate review of the references by the Examiner, a copy of the Information Disclosure Statement and the Form 1449 are attached hereto. A copy of the cited reference was provided at the time of filing the original Information Disclosure Statement, and, therefore, an additional copy of the reference is not submitted herewith. Applicants will be pleased to provide an additional copy upon the Examiner's request if it proves difficult to locate the original reference.

Applicant respectfully submits that all claims, as now submitted, are in condition for immediate allowance. Accordingly, a Notice of Allowance is respectfully requested in due course. If any minor formalities need to be addressed, the Examiner is directed to contact the undersigned attorney by telephone to facilitate prosecution of this case.

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It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

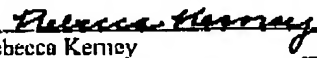
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CERTIFICATION OF FACSIMILE TRANSMISSION

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Rebecca Kenney

4/3/06
Date

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Substitute for form 1449/P10 (Revised 04/2003)				Complete if Known	
				Application Number	10/690,462
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Filing Date	October 21, 2003
				First Named Inventor	Snyder
				Group Art Unit	1624
				Examiner Name	V. Balasubramanian
				Attorney Docket Number	007157/270549
Sheet	1	of	1		

U. S. PATENT DOCUMENTS					
Examiner Initials*	Cite No.	Document Number Number - Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Chief Document	Pages, Columns, Lines, Where Relevant Passages of Relevant Figures Appear

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code - Number Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Chief Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	English Language Translation Attached

OTHER DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	English Language Translation Attached
	38	DIMMOCK <i>et al.</i> , "Evaluation of Some N-Acyl Analogues of 3,5-Bis(arylidene)-4-Piperidones for Cytotoxic Activity," <i>Drug Design and Discovery</i> , 1992, Vol. 8, pp. 291-299.	

Examiner Signature		Date Considered	
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*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. RTA01/2174255v1